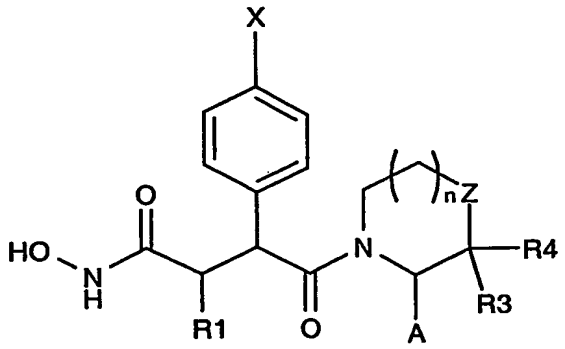
CLAIMS

1. A compound of Formula I



I

wherein

R_1 is lower alkyl, C_3-C_8cycloalkyl, C_3-C_{18}heterocycloalkyl or C_4-C_{18}aryl each of which is independently optionally substituted by hydroxy, halogen, lower alkoxy, C_3-C_8cycloalkyl-lower alkoxy, or C_4-C_{18} aryl-lower alkoxy;

X is halogen, cyano, lower alkyl, halo-substituted lower alkyl, C_4-C_{18}aryl, C_4-C_{18}aryl-lower alkyl, hydroxy, -OR_5, SR_5 or -NR_6R_7, each of which is optionally substituted by halogen, hydroxy, lower alkoxy, C_3-C_6cycloalkyl-lower alkoxy, or C_4-C_{18}aryl-lower alkoxy

wherein

R_5 is hydrogen, lower alkyl, C_3-C_8cycloalkyl, C_3-C_{18}heterocycloalkyl or C_4-C_{18}aryl

and

R_6 and R_7 are independently H, lower alkyl, C_3-C_8cycloalkyl, C_3-C_{18}heterocycloalkyl or C_4-C_{18}aryl;

Z is –CH_2-, -CHR_8-, -O-, -S-, or -$N(R_8)$-

wherein

R_8 is H, lower alkyl, C_3-C_8cycloalkyl, C_3-C_{18}heterocycloalkyl, C_4-C_{18}aryl lower alkoxycarbonyl or C_4-C_8aryloxycarbonyl, each of which is independently optionally substituted by halogen, hydroxy, lower alkoxy, C_3-C_6cycloalkyl-lower alkoxy, or C_4-C_8aryl-lower alkoxy ;

A is hydrogen, -$CR_{10}R_{11}$-Q-R_{12}, -C(O)-Q-R_{12} or -C(S)-Q-R_{12}

wherein

R_{10} and R_{11} are independently H, lower alkyl, C_3-C_8cycloalkyl, C_3-C_{18}heterocycloalkyl or C_4-C_{18}aryl each of which is independently optionally substituted by halogen, hydroxy, lower alkoxy, C_3-C_6cycloalkyl-lower alkoxy, or C_4-C_{18} aryl-lower alkoxy,

Q is $-NR_8-$, -S- or –O-, where R_8 is as defined above, and

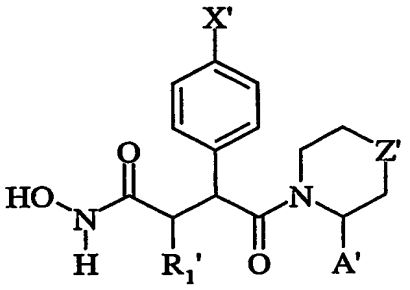
R_{12} is lower alkyl C_3-C_8cycloalkyl, C_4-C_{18}aryl, C_4-C_{18}aryl-lower alkyl, each optionally substituted by hydroxy, halogen, lower alkoxy, C_3-C_6cycloalkyl, C_3-C_6cycloalkoxy, C_4-C_{18}aryl or C_4-C_{18}aryl-lower alkoxy; and

R_3 and R_4 is Hydrogen or lower alkyl; and

n is 0 or 1,

or a pharmaceutically-acceptable and -cleavable ester thereof or acid addition salts thereof.

2. A compound according to claim 1of formula II



II

wherein

R_1' is H, lower alkyl or C_3-C_8cycloalkyl, each of which is optionally substituted by hydroxy, halogen, lower alkoxy or C_4-C_{18}aryl –lower alkoxy;

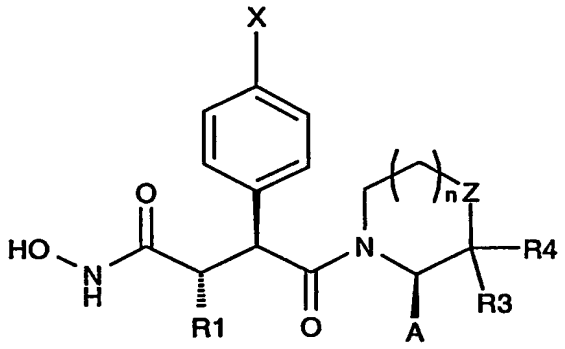
X' is halogen, cyano, lower alkyl, halo-substituted lower alkyl or lower alkoxy, each of which is optionally substituted by halogen, hydroxy or lower alkoxy;

Z' is $-CH_2-$ or $-N(R'_8)-$ wherein R'_8 is H, lower alkyl, C_4-C_{18}aryl (optionally substituted by halogen), lower alkoxycarbonyl or C_4-C_{18}aryloxycarbonyl;

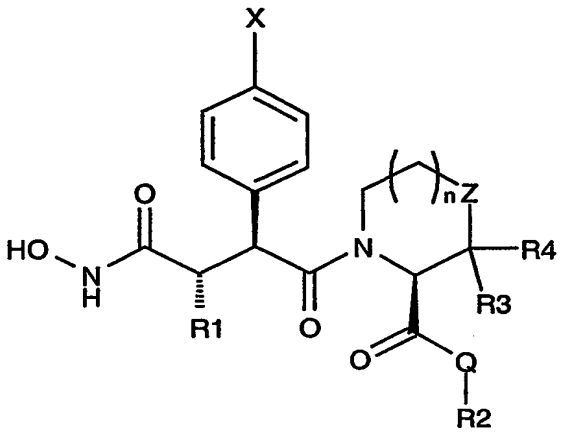
A' is H or $-C(O)-Q'-R_{12}$' wherein Q' is –S- or –O- and R_{12}' is lower alkyl, C_3-C_8 cycloalkyl, C_4-C_{18}aryl, each optionally substituted by hydroxy, halogen, lower alkoxy, C_3-C_8cycloalkyl, or C_4-C_{18}aryl,

or a pharmaceutically acceptable and cleavable ester thereof or acid addition salts thereof.

3. A compound according to claim 1 of formula I' or formula I''



I'



I''

wherein the symbols are as defined above
or a pharmaceutically acceptable and cleavable ester thereof or acid addition salts thereof.

4. A compound according to claim 1 selected from:
3(S)-(4-Chloro-phenyl)-2(S)-ethyl-N-hydroxy-4-morpholin-4-yl-4-oxo-butyramide;
2(R)-Benzyloxymethyl-4-[4-(4-chloro-phenyl)-piperazin-1-yl]-N-hydroxy-3(S)-(4-methoxy-phenyl)-4-oxo-butyramide;
2(R)-Benzyloxymethyl-N-hydroxy-3(S)-(4-methoxy-phenyl)-4-oxo-4-piperidin-1-yl-butyramide,
N-Hydroxy-2(R)-hydroxymethyl-3(S)-(4-methoxy-phenyl)-4-oxo-4-piperidin-1-yl-butyramide;

(S)-4-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-3-isobutylcarbamoyl-piperazine-1-carboxylic acid .tert.-butyl ester;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperazine-2-carboxylic acid isobutyl-amide trifluoro-acetate;

1-[4-Benzyloxy-3(R)-hydroxycarbamoyl-2(S)-(4-methoxy-phenyl)-butyryl]-piperidine-2(S)-carboxylic acid methylamide;

1-[4-Hydroxy-3(R)-hydroxycarbamoyl-2(S)-(4-methoxy-phenyl)-butyryl]-piperidine-2(S)-carboxylic acid methylamide;

1-[3(S)-Hydroxycarbamoyl-2(S)-(4-methoxy-phenyl)-pentanoyl]-piperidine-2(S)-carboxylic acid methylamide;

(S)-1-[(2S,3S)-3-Hydroxycarbamoyl-2-(4-methoxy-phenyl)-pentanoyl]-piperidine-2-carboxylic acid cyclopropylamide;

(S)-1-[(2S,3S)-3-Hydroxycarbamoyl-2-(4-methoxy-phenyl)-pentanoyl]-piperidine-2-carboxylic acid (2-methoxy-ethyl)-amide;

(S)-1-[(2S,3S)-3-Hydroxycarbamoyl-2-(4-methoxy-phenyl)-pentanoyl]-piperidine-2-carboxylic acid (4-hydroxy-cyclohexyl)-amide;

(S)-1-[(2S,3S)-3-Hydroxycarbamoyl-2-(4-methoxy-phenyl)-pentanoyl]-piperidine-2-carboxylic acid benzylamide;

(S)-1-[(2S,3S)-3-Hydroxycarbamoyl-2-(4-methoxy-phenyl)-pentanoyl]-piperidine-2-carboxylic acid (4-fluoro-phenyl)-amide;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperidine-2-carboxylic acid isopropylamide;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperidine-2-carboxylic acid cyclopropylamide;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperidine-2-carboxylic acid (3-isopropoxy-propyl)-amide;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperidine-2-carboxylic acid (4-hydroxy-cyclohexyl)-amide;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperidine-2-carboxylic acid benzylamide;

(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-piperidine-2-carboxylic acid phenylamide;

1-[3(S)-Hydroxycarbamoyl-2(S)-(4-methoxy-phenyl)-pentanoyl]-pyrrolidine-2(S)-carboxylic acid phenylamide;
(S)-1-[(2S,3S)-2-(4-Chloro-phenyl)-3-hydroxycarbamoyl-pentanoyl]-pyrrolidine-2-carboxylic acid ((S)-2-hydroxy-propyl)-amide;
or a pharmaceutically acceptable and cleavable ester thereof or acid addition salts thereof.

5. A method of inhibiting production of soluble TNF, inhibiting matrix metalloproteinase activity, or of reducing inflammation in a subject in need of such treatment which method comprises administering to said subject an effective amount of a compound according to claim 1.

6. A compound according to claim 1 for use as a pharmaceutical.

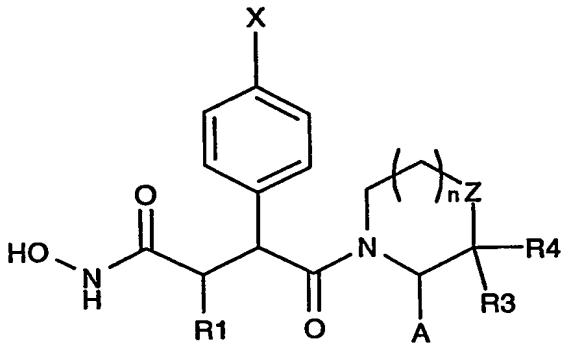
7. A pharmaceutical composition comprising a compound according to claim 1 in association with a pharmaceutically acceptable diluent or carrier.

8. Use of a compound according to claim 1 in the manufacture of a medicament for use as an immunosuppressant or anti-inflammatory agent.

9. A method of inhibiting neuropathic pain in a subject in need of such treatment which method comprises administering to said subject an effective amount of a compound according to claim 1.

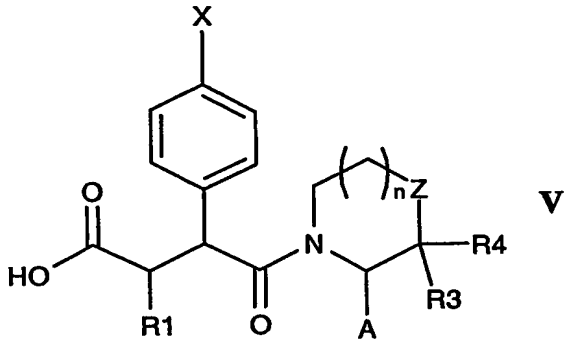
10 Use of a compound according to claim 1 in the manufacture of a medicament for use as a neuropathic pain relief agent or for use in the prevention, amelioration or treatment of neuropathic pain disease.

11. A process for the preparation of a compound of formula I



I

wherein the symbols are as defined above which comprises converting a corresponding free carboxylic acid derivative of formula V



V

wherein the symbols are as defined above, to the corresponding hydroxamic acid derivative of formula I.